



BAP1 tumor predisposition syndrome

BAP1 tumor predisposition syndrome is an inherited disorder that increases the risk of a variety of cancerous (malignant) and noncancerous (benign) tumors, most commonly certain types of tumors that occur in the skin, eyes, kidneys, and the tissue that lines the chest, abdomen, and the outer surface of the internal organs (the mesothelium). Affected individuals can develop one or more types of tumor, and affected members of the same family can have different types.

Some people with *BAP1* tumor predisposition syndrome develop growths in the skin known as atypical Spitz tumors. People with this syndrome may have more than one of these tumors, and they can have dozens. Atypical Spitz tumors are generally considered benign, although it is unclear if they can become cancerous. Skin cancers are also associated with *BAP1* tumor predisposition syndrome, including cutaneous melanoma and basal cell carcinoma.

A type of eye cancer called uveal melanoma is the most common cancerous tumor in *BAP1* tumor predisposition syndrome. Although uveal melanoma does not usually cause any symptoms, some people with this type of cancer have blurred vision; small, moving dots (floaters) or flashes of light in their vision; headaches; or a visible dark spot on the eye.

People with *BAP1* tumor predisposition syndrome are at risk of developing malignant mesothelioma, which is cancer of the mesothelium. When associated with *BAP1* tumor predisposition syndrome, malignant mesothelioma most often occurs in the membrane that lines the abdomen and covers the abdominal organs (the peritoneum). It less commonly occurs in the outer covering of the lungs (the pleura).

A form of kidney cancer called clear cell renal cell carcinoma is also associated with the condition. Researchers are still determining whether other forms of cancer are linked to *BAP1* tumor predisposition syndrome.

When they occur in people with *BAP1* tumor predisposition syndrome, cancers tend to arise at a younger age and are often more aggressive than cancers in the general population. The cancerous tumors in *BAP1* tumor predisposition syndrome tend to spread (metastasize) to other parts of the body. Survival of affected individuals with this syndrome is usually shorter than in other people who have one of these cancers. However, individuals with malignant mesothelioma as part of the *BAP1* tumor predisposition syndrome appear to survive longer than those who have the cancer without the syndrome.

Frequency

BAP1 tumor predisposition syndrome is a rare condition; its prevalence is unknown. More than 70 families with the condition have been described in the medical literature.

Genetic Changes

BAP1 tumor predisposition syndrome is caused by mutations in the *BAP1* gene. The BAP1 protein acts as a tumor suppressor, which means it helps prevent cells from growing and dividing too rapidly or in an uncontrolled way. Its function is to remove molecules called ubiquitin from certain proteins (deubiquitination), which can affect the activity of the protein and its interactions with other proteins. By removing ubiquitin, BAP1 helps regulate diverse cellular processes. The BAP1 protein is thought to be involved in cell growth and division (proliferation), cell death, repair of damaged DNA, and control of gene activity.

Mutations in the *BAP1* gene lead to production of an altered protein that cannot function normally and may be broken down prematurely. In addition to an inherited (germline) mutation in one copy of the gene, which is found in essentially every cell of the body, a second, non-inherited (somatic) mutation usually occurs in the normal copy of the gene in cells that give rise to tumors. Together, the germline and somatic mutations result in a complete loss of BAP1 protein function in tumor cells. A shortage of this protein's function likely impairs the removal of ubiquitin from certain proteins. Although it is unclear exactly how loss of BAP1 function leads to *BAP1* tumor predisposition syndrome, researchers speculate that altered activity of proteins normally regulated by BAP1 deubiquitination may promote cell proliferation or survival, resulting in tumor formation.

Studies suggest that environmental and lifestyle factors help determine which types of tumor develop in individuals with *BAP1* tumor predisposition syndrome. For example, exposure to asbestos likely contributes to the development of malignant mesothelioma. While asbestos increases the risk of malignant mesothelioma in the general population, the risk is even higher in individuals with a *BAP1* gene mutation. It is not clear why certain tumor types are particularly associated with *BAP1* tumor predisposition syndrome.

Inheritance Pattern

BAP1 tumor predisposition syndrome is inherited in an autosomal dominant pattern, which means one copy of the altered *BAP1* gene increases the chance of developing one or more tumors. In most cases, an affected person has one parent with the condition.

People with a mutation in the *BAP1* gene inherit an increased risk of tumor formation. Not all people with a gene mutation will develop a tumor.

Other Names for This Condition

- BAP1-related tumor predisposition syndrome
- BAP1-TPDS
- COMMON syndrome
- cutaneous/ocular melanoma, atypical melanocytic proliferations, and other internal neoplasms

Diagnosis & Management

Genetic Testing

- Genetic Testing Registry: Tumor susceptibility linked to germline BAP1 mutations
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C3280492/>

Other Diagnosis and Management Resources

- American Cancer Society: Treating Basal Cell Carcinoma
<https://www.cancer.org/cancer/basal-and-squamous-cell-skin-cancer/treating/basal-cell-carcinoma.html>
- Cancer.Net: Kidney Cancer: Treatment Options
<http://www.cancer.net/cancer-types/kidney-cancer/treatment-options>
- GeneReview: BAP1 Tumor Predisposition Syndrome
<https://www.ncbi.nlm.nih.gov/books/NBK390611>
- National Cancer Institute: Genetic Testing for Hereditary Cancer Syndromes
<https://www.cancer.gov/about-cancer/causes-prevention/genetics/genetic-testing-fact-sheet>
- National Cancer Institute: Intraocular (Uveal) Melanoma Treatment
<https://www.cancer.gov/types/eye/patient/intraocular-melanoma-treatment-pdq>
- National Cancer Institute: Malignant Mesothelioma Treatment
<https://www.cancer.gov/types/mesothelioma/patient/mesothelioma-treatment-pdq>
- National Cancer Institute: Melanoma Treatment
<https://www.cancer.gov/types/skin/patient/melanoma-treatment-pdq>

General Information from MedlinePlus

- Diagnostic Tests
<https://medlineplus.gov/diagnostictests.html>
- Drug Therapy
<https://medlineplus.gov/drugtherapy.html>
- Genetic Counseling
<https://medlineplus.gov/geneticcounseling.html>

- Palliative Care
<https://medlineplus.gov/palliativecare.html>
- Surgery and Rehabilitation
<https://medlineplus.gov/surgeryandrehabilitation.html>

Additional Information & Resources

MedlinePlus

- Health Topic: Cancer
<https://medlineplus.gov/cancer.html>
- Health Topic: Eye Cancer
<https://medlineplus.gov/eyecancer.html>
- Health Topic: Kidney Cancer
<https://medlineplus.gov/kidneycancer.html>
- Health Topic: Melanoma
<https://medlineplus.gov/melanoma.html>
- Health Topic: Mesothelioma
<https://medlineplus.gov/mesothelioma.html>

Additional NIH Resources

- National Cancer Institute: Intraocular (Uveal) Melanoma Treatment
<https://www.cancer.gov/types/eye/patient/intraocular-melanoma-treatment-pdq>
- National Cancer Institute: Malignant Mesothelioma Treatment
<https://www.cancer.gov/types/mesothelioma/patient/mesothelioma-treatment-pdq>
- National Cancer Institute: Melanoma Treatment
<https://www.cancer.gov/types/skin/patient/melanoma-treatment-pdq>

Educational Resources

- American Cancer Society: Kidney Cancer (Adult) - Renal Cell Carcinoma
<https://www.cancer.org/cancer/kidney-cancer/about/what-is-kidney-cancer.html>
- American Cancer Society: Skin Cancer: Basal and Squamous Cell
<https://www.cancer.org/cancer/basal-and-squamous-cell-skin-cancer/about/what-is-basal-and-squamous-cell.html>
- MalaCards: bap1-related tumor predisposition syndrome
http://www.malacards.org/card/bap1_related_tumor_predisposition_syndrome
- MD Anderson Cancer Center: Mesothelioma Facts
<https://www.mdanderson.org/cancer-types/mesothelioma/mesothelioma-facts.html>

- Orphanet: BAP1-related tumor predisposition syndrome
http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=289539
- University of Michigan Kellogg Eye Center: Uveal Melanoma (Eye Cancer)
<http://www.umkelloggeye.org/conditions-treatments/uveal-melanoma-eye-cancer>

Patient Support and Advocacy Resources

- American Cancer Society
<https://www.cancer.org/>
- Melanoma Research Foundation
<https://www.melanoma.org/>
- Ocular Melanoma Foundation
<http://www.ocularmelanoma.org/>
- Skin Cancer Foundation
<http://www.skincancer.org/skin-cancer-information/melanoma>

GeneReviews

- BAP1 Tumor Predisposition Syndrome
<https://www.ncbi.nlm.nih.gov/books/NBK390611>

ClinicalTrials.gov

- ClinicalTrials.gov
<https://clinicaltrials.gov/ct2/results?cond=%22BAP1+tumor+predisposition+syndrome%22>

Scientific Articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28BAP1+tumor+predisposition+syndrome%5BTIAB%5D%29+OR+%28BAP1+cancer+predisposition%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D>

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